

In re application of: **DULL ET AL.**

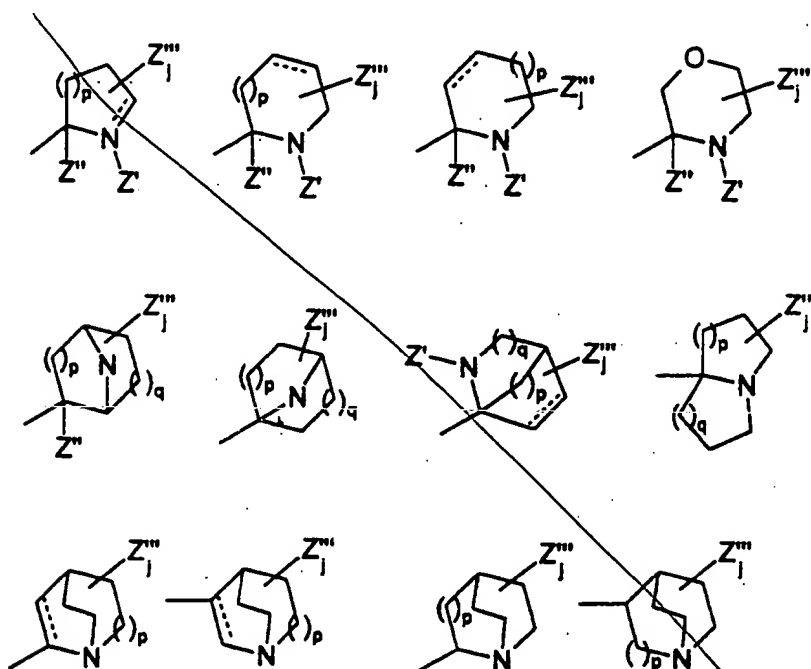
Serial No: **09/845,526**

Filed: **April 30, 2001**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

Examiner: **V. Balasubramanian**

Group Art Unit: **1624**



where Z' is hydrogen, lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3.

REMARKS

Claims 1-16, 22-41, 48-66 and 73-75 are pending. Claims 1, 16, 25, 41, 51 and 66 have been amended for clarity as suggested by the Examiner. None of the amendments presents new matter. The Examiner is respectfully requested to enter the amendments.

Applicants gratefully acknowledge that claims 1-16, 22-41 and 48-51 were indicated as allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, second paragraph. Applicants have amended the claims as suggested by the Examiner.

In re application of: **DULL ET AL.**

Serial No: **09/845,526**

Filed: **April 30, 2001**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

Examiner: **V. Balasubramanian**

Group Art Unit: **1624**

Rejections under 35 U.S.C. 112, Second Paragraph

Claims 1-16, 22-41, 48-66 and 73-75 have been rejected under 35 U.S.C. 112, second paragraph, as indefinite. Applicants respectfully traverse the rejections as applied to the amended claims.

The Office Action suggested that the term "aromatic group-containing species" was indefinite. Applicants have amended the claims to include a list of specific aromatic group-containing species. This list, which is disclosed in the specification at least on page 7, lines 5-6, includes phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl. Accordingly, the rejection should be withdrawn in light of the amendments to the claims.

The Office Action further suggested that the term "functionality" in the phrase "cycloalkyl functionality" should be replaced with "group." The claims have been amended as suggested by the Examiner. This amendment clarifies the subject matter being claimed but does not limit the claims in any manner.

The Office Action pointed out that claims 25-41 are composition claims that include only one element, namely the compound of interest. The claims have been amended as suggested by the Examiner to include, as a second element, a pharmaceutically acceptable carrier.

Rejections under 35 U.S.C. 112, First Paragraph

Claims 52-66 and 73-75 have been rejected under 35 U.S.C. 112, first paragraph, as non-enabled. Applicants respectfully traverse the rejections as applied to the amended claims.

Applicants gratefully acknowledge that the Office Action states that the claims are enabling for treating disorders associated with a dysfunction of nicotinic receptors. The claims have been amended as suggested by the Examiner to specify that the claims are directed to methods for treating disorders associated with a dysfunction of nicotinic receptors. This amendment is believed to obviate the rejections.

In re application of: **DULL ET AL.**

Serial No: **09/845,526**

Filed: **April 30, 2001**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

Examiner: **V. Balasubramanian**

Group Art Unit: **1624**

It is believed that the above-mentioned amendments and comments address each of the rejections. In light of the above-mentioned amendments and comments, Applicants respectfully request prompt issuance of a Notice of Allowance. Should the Examiner have any questions, the Examiner is invited to contact Applicants' undersigned representative at the telephone number below.

Respectfully submitted,

8/5/02
Date

David S. Bradin
David S. Bradin
Registration No. 37,783
Attorney for Applicant

Womble Carlyle Sandridge & Rice, PLLC
P.O. Box 13069
Research Triangle Park, North Carolina 27709
Phone: (919) 484-2382
Fax: (919) 484-2084

Docket No.: T103 1401.1
RTP 52692v1

In re application of: DULL ET AL.

Serial No: 09/845,526

Filed: April 30, 2001

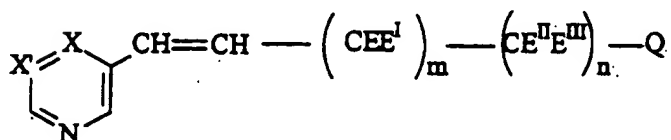
For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

Examiner: V. Balasubramanian

Group Art Unit: 1624

APPENDIX - AMENDED CLAIMS

1. (Twice Amended) A compound of the formula:



where X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, -OR', -NR'R'', -CF₃, -CN, -NO₂, -C₂R', -SR', -N₃, C(=O)NR'R'', -NR'C(=O)R'', -C(=O)R', -C(=O)OR', -OC(=O)R', -O(CR'R'')_rC(=O)R', -O(CR'R'')_rNR'R'', -O(CR'R'')_rNR'C(=O)R', -O(CR'R'')_rNR'SO₂R', -OC(=O)NR'R'', -NR'C(=O)OR'', -SO₂R', -SO₂NR'R'', and -NR'SO₂R'', where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E, E', E'' and E''' individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:

In re application of: **DULL ET AL.**

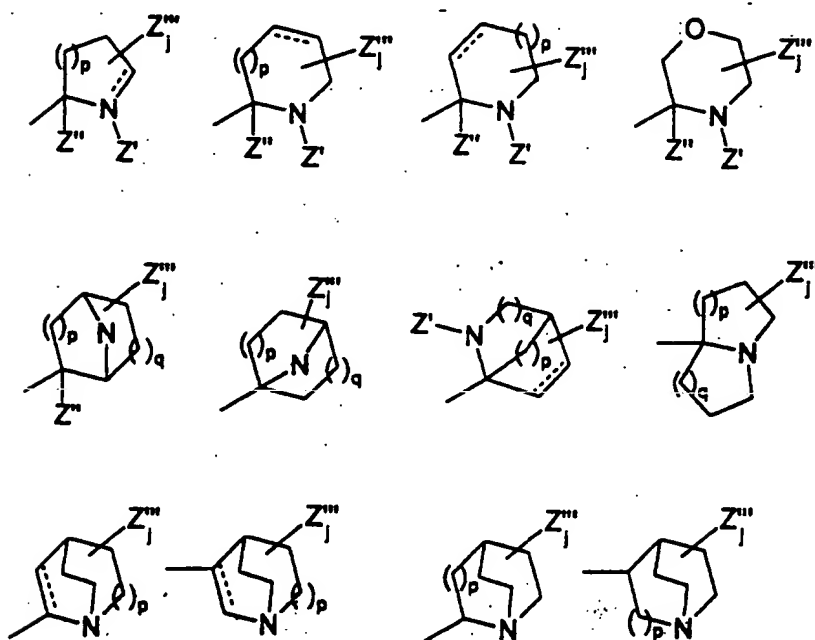
Serial No: **09/845,526**

Filed: **April 30, 2001**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

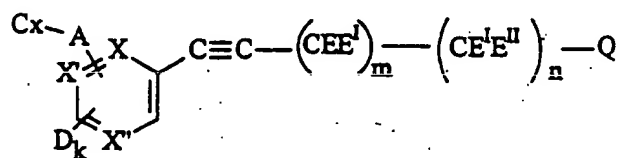
Examiner: **V. Balasubramanian**

Group Art Unit: **1624**



where Z' represents hydrogen or lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond, p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3.

16. (Twice Amended) A compound of the formula:



where X'' is individually nitrogen, X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, -OR', -NR'R'', -CF₃, -CN, -NO₂, -C₂R', -SR', -N₃, C(=O)NR'R'', -NR'C(=O)R'', -C(=O)R', -C(=O)OR', -OC(=O)R', -O(CR'R''), C(=O)R', -O(CR'R''), NR'R'', -O(CR'R''), NR'C(=O)R', -O(CR'R''), NR'SO₂R', -OC(=O)NR'R'', -NR'C(=O)O R'', -SO₂R', -SO₂NR'R'', and -NR'SO₂R'',

In re application of: DULL ET AL.

Serial No: 09/845,526

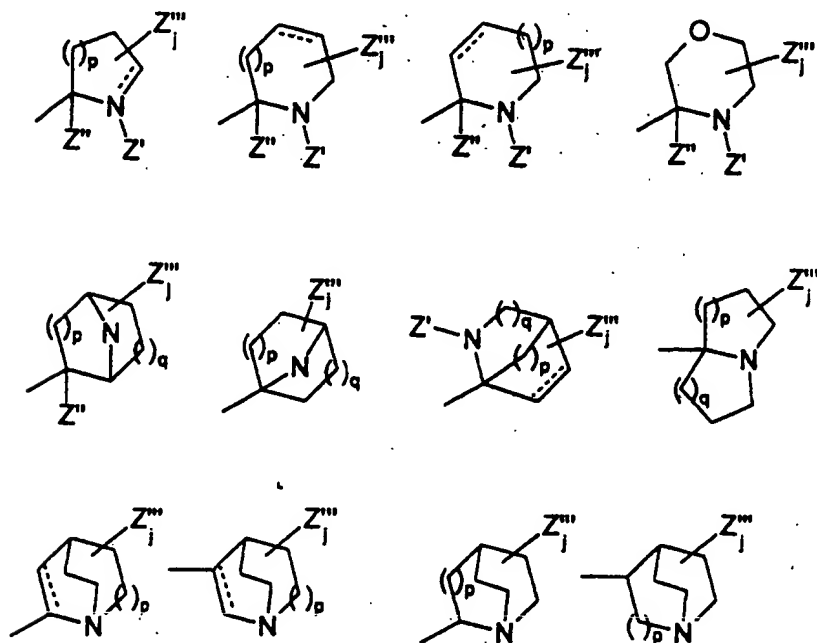
Filed: April 30, 2001

For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

Examiner: V. Balasubramanian

Group Art Unit: 1624

where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; A is O, C=O or a covalent bond; D is a suitable non-hydrogen substituent species selected from the group of substituent species for X, X' and X''; k is 0, 1 or 2; Cx is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic heterocyclylalkyl; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E, E', E'' and E''' individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:



where Z' represents hydrogen or lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3.

25. (Twice Amended) A pharmaceutical composition incorporating a compound of

In re application of: DULL ET AL.

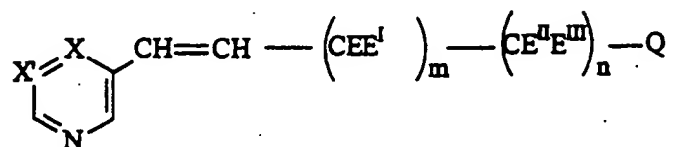
Serial No: 09/845,526

Filed: April 30, 2001

For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

Examiner: V. Balasubramanian

Group Art Unit: 1624



where X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, -OR', -NR'R'', -CF₃, -CN, -NO₂, -C₂R', -SR', -N₃, C(=O)NR'R'', -NR'C(=O)R'', -C(=O)R', -C(=O)OR', -OC(=O)R', -O(CR'R''), C(=O)R', -O(CR'R''), NR'R'', -O(CR'R''), NR''C(=O)R', -O(CR'R''), NR''SO₂R', -OC(=O)NR'R'', -NR'C(=O)OR'', -SO₂R', -SO₂NR'R'', and -NR'SO₂R'', where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E, E^I, E^{II} and E^{III} individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:

In re application of: DULL ET AL.

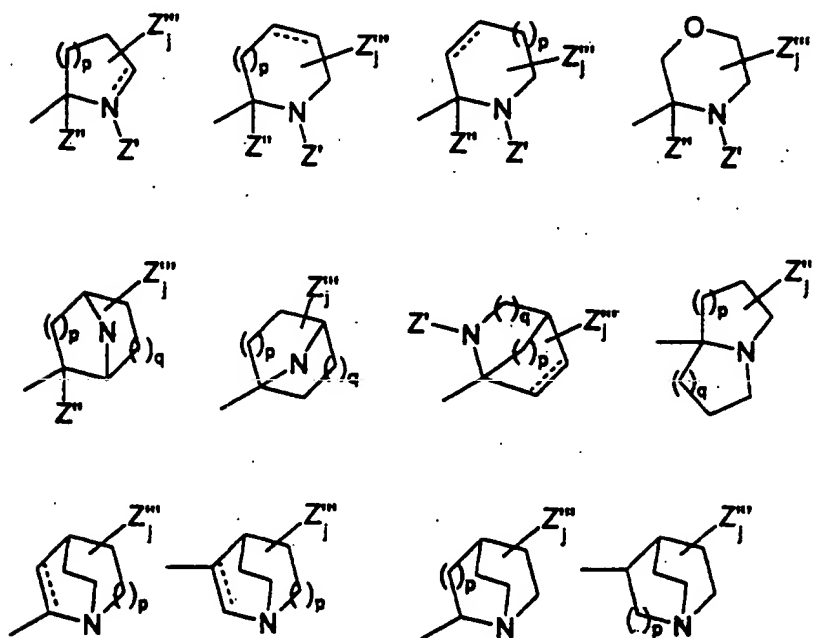
Serial No: 09/845,526

Filed: April 30, 2001

For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

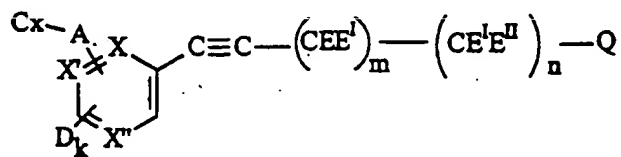
Examiner: V. Balasubramanian

Group Art Unit: 1624



where Z' represents hydrogen or lower alkyl, acyl, alkoxy carbonyl, or aryloxy carbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3, along with a pharmaceutically acceptable carrier.

41. (Twice Amended) A pharmaceutical composition incorporating a compound of the formula:



where X'' is nitrogen, X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, -OR', -NR'R'', -CF₃, -CN, -NO₂, -C₂R', -SR', -N₃, C(=O)NR'R'', -NR'C(=O)R'', -C(=O)R', -C(=O)OR', -OC(=O)R', -

In re application of: **DULL ET AL.**

Serial No: **09/845,526**

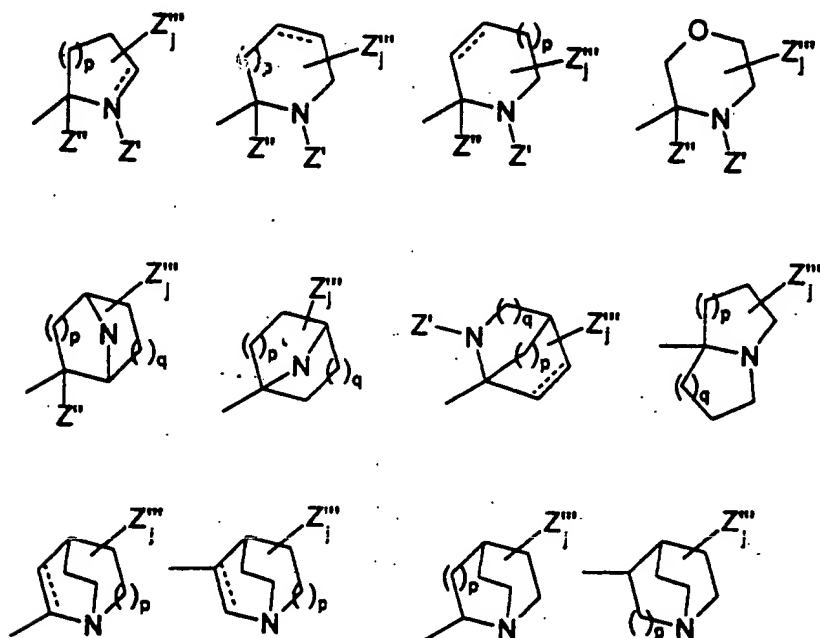
Filed: **April 30, 2001**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

Examiner: **V. Balasubramanian**

Group Art Unit: **1624**

$O(CR'R'')_rC(=O)R'$, $-O(CR'R'')_rNR'R''$, $-O(CR'R'')_rNR''C(=O)R'$, $-O(CR'R'')_rNR''SO_2R'$, $-OC(=O)NR'R''$, $-NR'C(=O)OR''$, $-SO_2R'$, $-SO_2NR'R''$, and $-NR'SO_2R''$, where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; A is O , $C=O$ or a covalent bond; D is a suitable non-hydrogen substituent species selected from the group of substituent species for X , X' and X'' ; k is 0, 1 or 2; C_x is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic hetero-cyclylalkyl; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E , E^I , E^{II} and E^{III} individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:



where Z' represents hydrogen or lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a

In re application of: DULL ET AL.

Serial No: 09/845,526

Filed: April 30, 2001

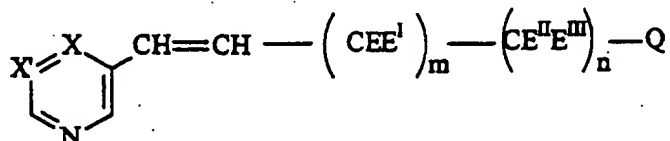
For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

Examiner: V. Balasubramanian

Group Art Unit: 1624

carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3, and a pharmaceutically acceptable carrier.

51. (Twice Amended) A method for treating a central nervous system disorder associated with dysfunction of nicotinic receptors, said method comprising administering an effective amount of a compound having the formula:



where X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, -OR', -NR'R'', -CF₃, -CN, -NO₂, -C₂R', -SR', -N₃, C(=O)NR'R'', -NR'C(=O)R'', -C(=O)R', -C(=O)OR', -OC(=O)R', -O(CR'R''), C(=O)R', -O(CR'R''), NR'R'', -O(CR'R''), NR''C(=O)R', -O(CR'R''), NR''SO₂R', -OC(=O)NR'R'', -NR'C(=O)OR'', -SO₂R', -SO₂NR'R'', and -NR'SO₂R'', where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E, E', E'' and E''' individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:

In re application of: **DULL ET AL.**

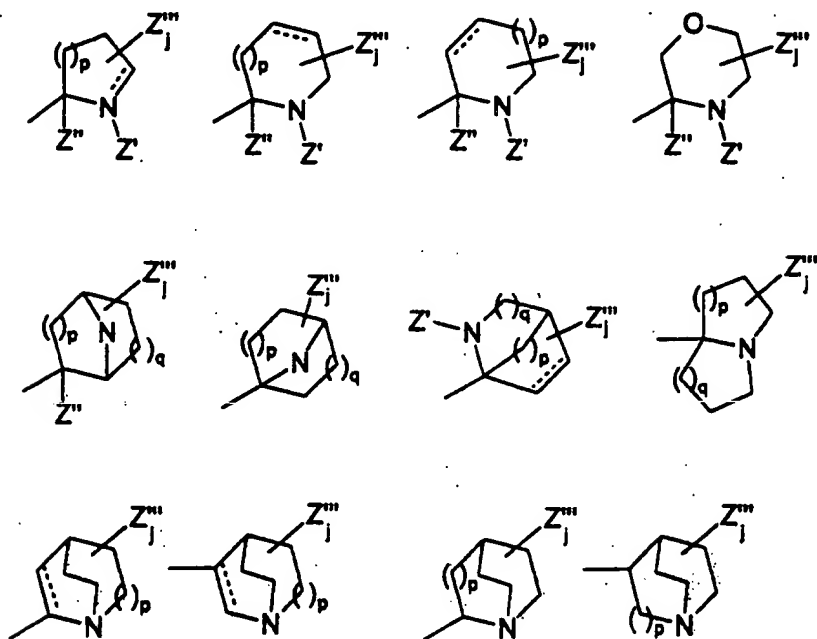
Serial No: 09/845,526

Filed: April 30, 2001

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

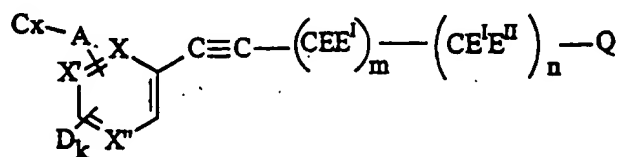
Examiner: **V. Balasubramanian**

Group Art Unit: 1624



where Z' is hydrogen, lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3.

66. (Twice Amended) A method for treating a central nervous system disorder associated with dysfunction of nicotinic receptors, said method comprising of the administration of an effective amount of a compound having the formula:



where X'' is nitrogen, X and X' are individually carbon bonded to a substituent species selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl; arylalkyl, substituted arylalkyl, halo, $-OR'$, $-NR'R''$, $-CF_3$, $-CN$, -

In re application of: DULL ET AL.

Serial No: 09/845,526

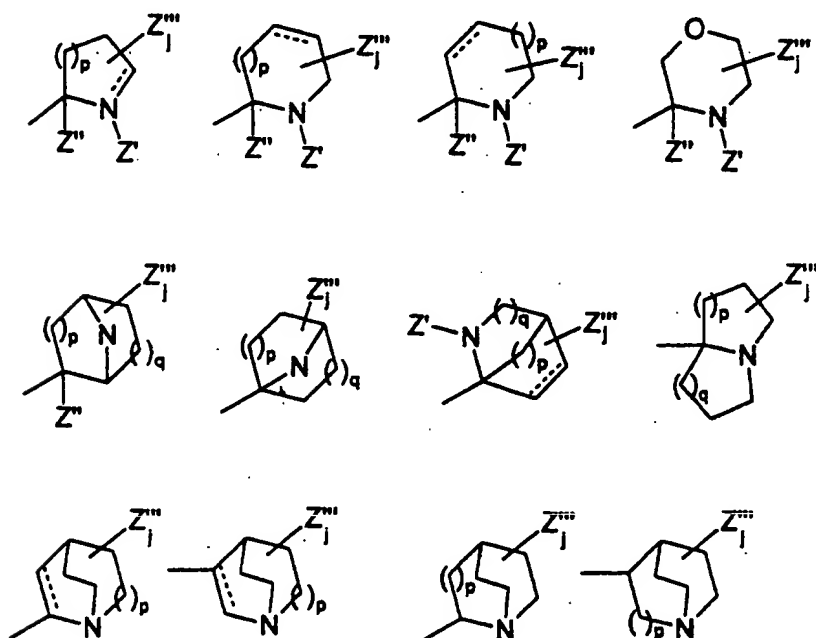
Filed: April 30, 2001

For: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE

Examiner: V. Balasubramanian

Group Art Unit: 1624

NO_2 , $-\text{C}_2\text{R}'$, $-\text{SR}'$, $-\text{N}_3$, $\text{C}(=\text{O})\text{NR}'\text{R}''$, $-\text{NR}'\text{C}(=\text{O})\text{R}''$, $-\text{C}(=\text{O})\text{R}'$, $-\text{C}(=\text{O})\text{OR}'$, $-\text{OC}(=\text{O})\text{R}'$, $-\text{O}(\text{CR}'\text{R}'')_r\text{C}(=\text{O})\text{R}'$, $-\text{O}(\text{CR}'\text{R}'')_r\text{NR}'\text{R}''$, $-\text{O}(\text{CR}'\text{R}'')_r\text{NR}''\text{C}(=\text{O})\text{R}'$, $-\text{O}(\text{CR}'\text{R}'')_r\text{NR}''\text{SO}_2\text{R}'$, $-\text{OC}(=\text{O})\text{NR}'\text{R}''$, $-\text{NR}'\text{C}(=\text{O})\text{O R}''$, $-\text{SO}_2\text{R}'$, $-\text{SO}_2\text{NR}'\text{R}''$, and $-\text{NR}'\text{SO}_2\text{R}''$, where R' and R'' are individually hydrogen, lower alkyl, cycloalkyl, heterocyclyl, or an aromatic group-containing species selected from the group consisting of phenyl, benzyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl and quinolinyl, and r is an integer from 1 to 6, or R' and R'' can together form a cycloalkyl [functionality] group; A is O , $\text{C}=\text{O}$ or a covalent bond; D is a suitable non-hydrogen substituent species selected from the group of substituent species for X , X' and X'' ; k is 0, 1 or 2; C_x is selected from a group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, non-aromatic heterocyclyl, substituted non-aromatic heterocyclyl, non-aromatic heterocyclylalkyl and substituted non-aromatic hetero-cyclylalkyl; m is an integer and n is an integer such that the sum of m plus n is 0, 1, 2 or 3; E , E^I , E^{II} and E^{III} individually represent hydrogen or a suitable non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl; and Q is selected from:



where Z' is hydrogen, lower alkyl, acyl, alkoxycarbonyl, or aryloxycarbonyl; Z'' is hydrogen or lower alkyl; and Z''' is a non-hydrogen substituent selected from the group consisting of alkyl, substituted alkyl, halo-substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, arylalkyl and substituted arylalkyl;

In re application of: **DULL ET AL.**

Serial No: **09/845,526**

Examiner: **V. Balasubramanian**

Filed: **April 30, 2001**

Group Art Unit: **1624**

For: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR USE**

substituted arylalkyl; the dotted line indicates a carbon-carbon single bond or a carbon-carbon double bond; p is 0, 1 or 2; q is 0, 1, 2 or 3; and j is an integer from 0 to 3.